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INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

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Applicant's or agent's file reference JAB1714f-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/50241	International filing date (day/month/year) 19.06.2003	Priority date (day/month/year) 24.06.2002
International Patent Classification (IPC) or both national classification and IPC C07D295/15		
Applicant JANSSEN PHARMACEUTICA N.V. et al		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 17.12.2003	Date of completion of this report 23.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer O'Sullivan, P Telephone No. +31 70 340-4511 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/50241

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-7 as originally filed

Claims, Numbers

1-7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/50241

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-7
	No: Claims	
Inventive step (IS)	Yes: Claims	1-7
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-7
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 96/40664 A

D2: US-A-3 953 448

Novelty (Art 33(2) PCT)

The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (page 11, lines 1-14) a process for the preparation of N-lidocaine. The difference between D1 and present claim 1 are 1) the use of an equimolar amount of hydrochloric acid with regard to the piperazine in the present application and none in D1, 2) the use of a 10-fold excess of piperazine in D1 and a 1 to 6-fold excess in the present application 3) the use of an organic solvent in D1 and an aqueous solvent in the present application and 4) the method of isolating the product.

Present claim 1 and therefore dependent claims 2-7 are novel over D1.

D2 discloses (column 12, line 53-column 4, line 17) a process for the production of the same product which differs in that the piperazine is monoprotected for the coupling reaction and subsequently deprotected to yield the desired product in two separate steps. Claim 1 and therefore claims 2-6 are novel over D2.

Inventive Step (Art 33(3) PCT)

The problem to be solved by the present invention may be regarded as the provision of an improved process for the production of N-lidocaine in which the problems associated with the need in the prior art to fully remove solvent and the isolation of the product as an oil (application, page 2, lines 1-8) are avoided.

The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step because there is no teaching nor incentive in the prior art documents D1 and D2 which would lead the skilled person to make the necessary changes to the processes of D1 or D2 in order to arrive at the present solution proposed by the claims.